homologous to nucleotides 1232-2207 of SEQ ID NO:1. The Office Action indicates further that the fragment could be composed of 85% disclosed sequence and 15% undisclosed sequence. The Office Action indicates further that if a probe/primer were derived from the fragment, it may be derived from the 15% undisclosed sequence, and therefore the sequence of the probe/primer would not have been disclosed in the present specification. However, Applicants respectfully submit that this interpretation of claims 5 and 8 is incorrect.

Claims 5 and 8 are directed to a probe/primer having at least 85% homology with a fragment of a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1.

The claimed probe/primer is not derived from a fragment that is 85% homologous to a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1. In contrast, the probe/primer itself is at least 85% homologous to a fragment of a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1. Accordingly, the probe/primer sequence will always share at least 85% homology with a fragment of the disclosed sequence.

Although the claims further recite that the probe/primer has at least 5 and no more than 100 or 30 nucleotides, respectively, these features do not change the fact that the claimed probe/primer is at least 85% homologous with a fragment of a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1.

For at least these reasons, Applicants submit that it would be clear to one skilled in the art that the claimed probe/primer is 85% homologous to a sequence disclosed in the present specification. Accordingly, claims 5 and 8 are not indefinite and are not vague and confusing to one of ordinary skill in the art.

The Office Action indicates that claim 10 is dependent upon canceled claim 9. By this Amendment, claim 10 is amended to correctly depend from pending claim 8.

The Office Action indicates that claims 18, 19 and 27 are vague and indefinite for failing to state the exact hybridization conditions. Applicants respectfully disagree.

Claims 18, 19 and 27 are directed to a method/process for detection and/or identification of *T. cruzi* in a biological sample that involves hybridization of a probe to the target nucleic acid. Claims 18, 19 and 27 are clear and definite in that they claim a method/process for detection and/or identification of *T. cruzi* in a biological sample that involves hybridization of a probe to the target nucleic acid.

Hybridization is a commonly used, well-known molecular biology method. The absence of exact hybridization conditions in claims 18, 19 and 27 does not render these claims indefinite because one of ordinary skill in the art would know conditions that would be appropriate to perform the claimed hybridization.

For at least these reasons, Applicants submit that claims 18, 19 and 27 are not vague and indefinite to one of ordinary skill in the art.

The Office Action indicates that claims 21-23 are vague and indefinite for reciting the phrase "wherein each segment of 30 contiguous nucleotides of said nucleotide sequence has at least 85% homology with a segment of 30 contiguous nucleotides of said reference sequence." The Office Action also indicates that the length of the claim sequence is unclear. Applicants submit that claims 21-23 are not vague and indefinite.

Claims 21-23 are directed to a nucleic acid fragment comprising a nucleotide sequence having at least 85% homology with a specifically defined reference sequence, wherein each segment of 30 contiguous nucleotides of the nucleotide sequence has at least 85% homology with a segment of 30 contiguous nucleotides of the reference sequence. Since these claims clearly recite a sequence that has at least 85% homology with the

reference sequence, the claimed sequences are clearly at least 85% of the length of the reference sequence. It is respectfully submitted that this would be understood by one of ordinary skill in the art.

The additional limitation: "wherein each segment of 30 contiguous nucleotides of said nucleotide sequence has at least 85% homology with a segment of 30 contiguous nucleotides of said reference sequence" would not be confusing to one of ordinary skill in the art. This phrase further limits the claimed sequence. In addition to the claimed sequence being at least 85% homologous to the reference sequence, this limitation requires that every segment of 30 consecutive nucleotides be at least 85% homologous to a corresponding segment of 30 consecutive nucleotides of the reference sequence.

In other words, in addition to the entire claimed sequence being at least 85% homologous to the reference sequence, every segment of 30 contiguous nucleotides of the claimed sequence must be at least 85% homologous to a segment of 30 contiguous nucleotides of the reference sequence. Since the claims recite that <u>each</u> segment has this feature, these segments are clearly not spaced apart.

For at least these reasons, Applicants submit that claims 21-23 are not vague and indefinite to one of ordinary skill in the art.

The Office Action indicates that the feature "said nucleotide sequence (a)" of claims 36-38 allegedly lacks antecedent basis. Applicants respectfully disagree.

Claims 36-38 claims a sequence of a nucleic acid fragment that is either identical to or is a degenerate sequence of a reference sequence, <u>or</u> is a full complement of the reference sequence. The designations (a) and (b) in claims 36-38 were intended to clearly distinguish these two alternatives, and were not in-and-of-themselves references to a sequence. However, these designations have been removed in order to eliminate confusion, and the contents of these two subsections have been separated into individual paragraphs.

For at least these reasons, Applicants submit that each feature of claims 36-38 has proper antecedence.

The Office Action does not directly address claims 7, 11-17, 20, 24-26, 32, 34, 39 and 40. Applicants assume that these dependent claims are rejected for the same reasons that their respective base claims are rejected. Accordingly, Applicants submit that these claims are not indefinite for at least the reasons discussed above, for claims 5, 8, 10, 18, 19, 21-23, 27 and 36-38.

For at least the reasons discussed above, Applicants submit that claims 5, 7, 8, 10-26, 32, 34 and 36-40 satisfy the requirements of 35 U.S.C. §112, second paragraph. Reconsideration and withdrawal of the rejection are respectfully requested.

II. NEW MATTER

Claims 5, 7, 8, 11-20, 25, 26, 32, 34 and 36-40 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse the rejection.

Claims 5, 7, 8, 11-20, 25, 26, 32, 34, 39 and 40 are directed to a probe/primer for identifying Trypanosoma cruzi, said probe having at least 85% homology with a fragment of a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1, wherein said probe contains at least 5 and no more than 100 nucleotides and said primer contains at least 5 and no more than 30 nucleotides. Support for these claims can clearly be found at, for example, page 15, lines 15-24, of the present application.

The specification defines the claimed nucleotide sequence (i.e., the nucleotide sequence with which the probe/primer has 85% homology) as nucleic acids having a

nucleotide sequence as represented in the identified SEQ ID NO: 1 or a complementary sequence to SEQ ID NO: 1. See page 15, lines 18-20. The specification indicates that, for any succession of 5 to 100 contiguous monomers, the probe/primer can have at least 85% homology with fragments of SEQ ID NO: 1 or a complementary sequence to SEQ ID NO: 1. See page 15, lines 21-24.

For these reasons, Applicants submit that page 15, lines 15-14, of the present specification provides support for the claimed probes/primers having at least 85% homology to fragments of SEQ ID NO: 1 or a complementary sequence to SEQ ID NO: 1.

Regarding claims 36-38, the Office Action indicates that support could not be found for the feature "degenerates." Support for degenerates can be found in the present specification at, for example, on page 6, lines 26-29, which indicates that the nucleotide fragment of the present invention can be any fragment containing at least 30 contiguous nucleotides encoding a peptide homologous or identical to the peptide encoded by the specified reference sequence.

For at least these reasons, Applicants submit that the subject matter of claims 36-38 is described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

For at least the reasons discussed above, Applicants submit that claims 5, 7, 8, 11-20, 25, 26, 32, 34 and 36-40 do not contain new matter. Reconsideration and withdrawal of the rejection are respectfully requested.

III. ENABLEMENT

Claims 5, 7, 8, 10-27, 32, 34 and 36-40 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification

in such a way as to enable one skilled in the art to make and/or use the invention. Applicants respectfully traverse the rejection.

Claims 29, 31, 33 and 35 are not currently pending. These four claims were canceled in the Preliminary Amendment, which was acknowledged by this Office Action.

According to 35 U.S.C. §112, first paragraph, the specification must provide sufficient information to make and use the claimed invention without undue experimentation. It is respectfully submitted that the specification provides such sufficient disclosure to support the present claims, as properly construed.

In particular, as discussed in section I above, claims 5 and 8 are each clearly directed to a probe or primer that is at least 85% homologous to a fragment of a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1. Accordingly, the claimed probe/primer sequence will always share at least 85% homology with a disclosed sequence. The claimed probes and primers are not merely derived from a sequence having at least 85% homology with the claimed reference sequences.

In addition, as also discussed in section I above, claims 21-24 are clearly directed to a nucleotide sequence that has at least 85% homology with a reference sequence. Claims 21-24 also recite that each segment of 30 contiguous nucleotide of the nucleotide sequence have at least 85% homology with a segment of 30 contiguous nucleotides of the reference sequence. Thus, these claims clearly do not encompass sequences that are 70-95% different from the defined reference sequences. Instead, they must comprise a sequence having at least 85% homology with the reference sequence.

It is respectfully submitted that this subject matter is enabled by the present specification. In particular, it would be within the skill of the art to use fragments having at least 85% homology to a reference sequence as a probe or primer. It is well known in the art

that two nucleotide sequences do not have to be 100% homologous (i.e., identical) to hybridize to one another. One of ordinary skill in the art would understand that a fragment having 85% homology to the reference sequence can be successfully hybridized to the reference sequence. This is true regardless of which nucleotides are added, subtracted or deleted. Therefore, further guidance in the specification is not required to practice the claimed invention.

Claims 21-23 indicate that every segment of 30 contiguous nucleotides must be at least 85% homologous with a corresponding 30 contiguous nucleotides of the reference sequence. This serves to further limit the nucleotides that can be changed and still be within the scope of claims 21-23.

In addition, also as discussed in section I above, claims 18, 19 and 27 are clearly directed to methods for detection and/or identification of Trypanosoma cruzi in a biological sample comprising hybridizing probe to a target sequence. It is respectfully submitted that this subject matter is enabled by the present specification. In particular, it would be well within the skill of the art to hybridize a probe to a target sequence.

The Office Action indicates that these claims are not enabled because they fail to recite specific hybridization conditions to be used in the methods, and because of an alleged lack of guidance in the specification. Applicants respectfully disagree.

Nucleic acid hybridization is a conventional molecular biology technique that is used extensively by those skilled in the art. Thus, it is not necessary for the specification to provide specific guidance as to how the claimed probes and primers can be used to detect and identify Trypanosoma cruzi by hybridization techniques. In particular, one of ordinary skill in the art is well aware of appropriate hybridization conditions that could be used to conduct such an assay and would be able to select specific conditions with only routine

experimentation. Thus, Applicants submit that the claims are not required to recite exact hybridization conditions in order to enable one skilled in the art to use the claimed invention.

In addition, *In re W.L. Gore and Assoc.* and *In re Johnson* established that one does not look to the claims but to the specification to find out how to practice the claimed invention. *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1558, 220 USPQ 303, 316-317 (Fed. Cir. 1983); *In re Johnson*, 558 F.2d 1008, 1017, 194 USPQ 187, 195 (CCPA 1977). Contrary to the indication in the Office Action, the specification does provide guidance as to how to practice the claimed methods.

In particular, on page 36, lines 1-7, of the specification, Applicants indicate that the conventional molecular biology techniques disclosed in the present specification (such as hybridization assays) were performed according to the procedures disclosed in Maniatis et al. (Maniatis). One of ordinary skill in the art would be familiar with Maniatis. Maniatis has been the mainstay of molecular biology for nearly 20 years. Maniatis has an unrivaled reputation for reliability, accuracy and clarity. Those skilled in the art recognize that Maniatis describes molecular biology techniques that are used every day in laboratories for isolating, analyzing and cloning nucleic acid molecules. In particular, Maniatis discloses techniques for amplification of DNA/RNA and the generation and use of nucleic acid probes. Maniatis is known for also explaining why techniques work, how they were developed, and how they have evolved.

Those skilled in the art recognize that Maniatis has extensive coverage of nearly all core molecular biology techniques and often present several different means of accomplishing the same goal. Further, Maniatis is known for its extensive troubleshooting section, considered by many to be an invaluable resource.

The present specification clearly indicates that the probes of the present invention can be used in any known hybridization techniques. The specification lists Dot-Blots, Southern

Blots and Northern Blots as examples, and cites Maniatis, Southern et al. and Dunn et al. as reliable sources for the specific protocols. See page 16, line 27 to page 17, line 3. All of the methods needed to practice the claimed invention are well known, and there was a high level of skill in the art at the time the present application was filed. Further, as indicated in Example 4 and page 36, Applicants successfully practiced the claimed invention by using the protocols disclosed in Maniatis.

Therefore, one of ordinary skill in the art would be able to select the appropriate conditions for the well-known technique of hybridization, based on the present disclosure and the protocols outlined in Maniatis, without undue experimentation.

The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'." *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Based on the present specification, practicing the present invention would not involve undue experimentation. Instead, any necessary experimentation would be considered routine in the art. Thus, the fact that some experimentation may be required to practice the present invention does not render the present specification non-enabling.

For at least these reasons, Applicants submit that claims 18, 19 and 27 claim subject matter that was described in the specification in such a way as to enable one skilled in the art to use the claimed invention.

Claims 7, 10-17, 25-26, 32, 39 and 40 ultimately depend from claims 5 or 8. Claims 24 and 36-38 ultimately depend from claims 21, 22 or 23. Claims 20 and 34 ultimately depend from claims 18 or 19. These dependent claims are enabled for at least the reasons discussed above for independent claims 5, 8, 18, 19 and 21-23.

Accordingly, Applicants submit that the subject matter of claims 5, 7, 8, 10-27, 32, 34 and 36-40 is described in the specification sufficiently to enable one of ordinary skill in the

art to make/use the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

IV. WRITTEN DESCRIPTION

Claims 5, 7, 8, 10-27, 32, 34 and 36-40 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse the rejection.

According to 35 U.S.C. §112, first paragraph, the specification must contain a written description of the invention. To satisfy the written description requirement, the specification must describe the invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, for example, *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). It is respectfully submitted that the specification provides such sufficient disclosure to support the present claims, as properly construed. The proper construction of the claims is discussed in detail in sections I and III above.

As indicated in University of California v. Eli Lilly & Co., 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997), which is relied upon in the Office Action, an adequate written description of a DNA "requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Specifically, in Eli Lilly, the Federal Circuit held that a claim directed to human insulin cDNA was not adequately supported by the specification, which merely identified the cDNA by its principle biological activity, i.e., encoding human insulin, and a potential method for isolating it, without describing any structural features of the cDNA. 119 F.3d at 1567, 43 USPQ2d at 1404-05. In addition, the Federal Circuit held that the description

of rat insulin cDNA was insufficient to support claims that generically recite vertebrate or mammalian insulin cDNA, which would, of course, encompass human as well as rat cDNA. Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1405.

Thus, in Eli Lilly, the Federal Circuit held that providing no structural information about the claimed human DNA was insufficient. However, the Federal Circuit has not held that it is necessary to set forth an exact nucleotide sequence for any sequence within the claim, much less for more than one embodiment within a claim, in order to fulfill the written description requirement, as is suggested in the Final Rejection.

In fact, Eli Lilly clearly supports the opposite conclusion stating that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties," clearly indicating that something other than the exact formula can be sufficient to precisely define and thus provide written description for a nucleic acid.

Instead, what is required for written description is a precise definition of the nucleic acid "sufficient to distinguish [the claimed material] from other materials." Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1405. The present specification provides a precise definition of the claimed nucleic acid in a manner that is sufficient to distinguish the claimed nucleic acids from other nucleic acids.

Unlike the situation in Eli Lilly, the present specification clearly provides more than a mere statement that the claimed nucleotide sequences are part of the invention and reference to a potential method for isolating them. Instead, the specification clearly indicates that the inventors isolated and sequenced the nucleotide sequence of SEQ ID NO: 1 and specifically describes the fragments thereof identified in the present claims.

In addition to describing this specific sequence, the specification specifically describes nucleotide sequences having at least 85% homology with SEQ ID NO: 1, or a fragment thereof, or a sequence that can hybridize to SEQ ID NO: 1. Reference to these

nucleotide sequences clearly provides substantial structural information about all of the sequences recited within the claims. In particular, the specification provides sufficient structural information to distinguish the claimed nucleic acids from nucleic acids that are outside the scope of the claims, as was required by the Federal Circuit in Eli Lilly.

That is, even though the specification does not set forth the nucleotide sequence of every nucleic acid within the claims, one could easily identify by its nucleotide sequence whether a particular nucleic acid displays at least 85% homology with SEQ ID NO: 1, or a fragment thereof, or a sequence that can hybridize to SEQ ID NO: 1, and is thus within the scope of the present claims.

As a result, the present situation can clearly be distinguished from the situation in Eli Lilly where a nucleic acid was identified merely by its principle biological activity. Instead, in the present case, the claimed nucleic acids are identified by distinguishing structural characteristics. Thus, it is respectfully submitted that the specification clearly provides written description supporting the present claims.

For at least these reasons, Applicants submit that the subject matter of claims 5, 7, 8, 10-27, 32, 34 and 36-40 was described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

V. CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 5, 7, 8, 10-26, 32, 34 and 36-40 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below.

Respectfully submitted,

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WPB:PAC/hs

Attachment:
Appendix

Date: June 21, 2002

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE AUTHORIZATION
Please grant any extension necessary for entry;
Charge any fee due to our Deposit Account No. 15-0461

APPENDIX

Changes to Claims:

The following are marked-up versions of the amended claims:

10. (~~Twice~~ Three Times Amended) The primer according to claim ~~9~~8, wherein said primer comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10 and SEQ ID NO:12.

36. (Amended) The nucleic acid fragment of claim 21, wherein said nucleotide sequence: ~~(a)~~

_____is a nucleic acid sequence that is identical to or is a degenerate of a sequence starting at nucleotide 1232 and ending at nucleotide 1825 of SEQ ID NO: 1 or the corresponding RNA sequence, or ~~(b)~~

_____-is a full complement of said nucleic acid sequence.

37. (Amended) The nucleic acid fragment of claim 22, wherein said nucleotide sequence: ~~(a)~~

_____is a nucleic acid sequence that is identical to or is a degenerate of a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1 or the corresponding RNA sequence, or ~~(b)~~

_____is a full complement of said nucleic acid sequence.

38. (Amended) The nucleic acid fragment of claim 23, wherein said nucleotide sequence: ~~(a)~~

_____is a nucleic acid sequence that is identical to or is a degenerate of a sequence starting at nucleotide 1266 and ending at nucleotide 2207 of SEQ ID NO: 1 or the corresponding RNA sequence, or ~~(b)~~

_____is a full complement of said nucleic acid sequence.